

## REMARKS

Claims 1-23 were filed in the original application. New Claim 24 is added herein. Support for the recited "cartridge configured to hold a plurality of nucleic acid synthesis columns" is found throughout the specification, *e.g.*, at page 3, lines 1-2. The term "cartridge" is further described at page 23, lines 3-9.

### **Claim Rejections**

Claims 2 and 11-14 were rejected under 35 U.S.C. §112(2). Claims 1-4, and 11-20 were rejected under 35 U.S.C. §102(b) and (e). Claims 5-10, and 21-23 were rejected under 35 U.S.C. §103(a). The rejections are discussed below.

#### **I. Rejections Under 35 U.S.C. §112(2)**

The Examiner rejects Claims 2 and 11-14 under 35 U.S.C. §112(2) "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Office Action, page 2. The Applicants respectfully disagree. However, without acquiescing to the Examiner's arguments, and in order to expedite prosecution, Claims 2 and 11-14 are now canceled. As such, these rejections are rendered moot. The Applicants reserve the right to prosecute these or similar claims in the future.

#### **II. Rejections Under 35 U.S.C. §102(b) And §102(e)**

##### **A. Claims 2-4 and 11-19 Are Rejected Under 35 U.S.C. §102(b) and (e)**

The Examiner rejects Claims 2-4 and 11-19 under 35 U.S.C. §102(b) and (e). Office Action, pages 2-4. The Applicants respectfully disagree. However, without acquiescing to the Examiner's arguments, and in order to expedite prosecution, Claims 2-4 and 11-19 are now canceled. As such, these rejections are rendered moot. The Applicants reserve the right to prosecute these or similar claims in the future.

##### **B. Claim 1 Is Not Anticipated By DeWitt Or McGowan**

The Examiner rejects Claim 1 as being anticipated by U.S. Patent Nos. 5,702,672 (hereinafter "DeWitt") and 6,238,627 (hereinafter "McGowan"). The Applicants respectfully disagree. A claim is not anticipated by a prior reference when that reference fails to describe

each and every element as set forth in the contested claim. *Verdegall Bros. v. Union Oil Co. of California*, 814 F.2d 628 (Fed.Cir. 1987). Here, Claim 1 is directed to an oligonucleotide synthesizer. DeWitt and McGowan, however, each fail to describe oligonucleotide synthesizers as described in Claim 1. As such, Claim 1 is not anticipated by DeWitt or McGowan. However, in order to expedite prosecution, Claim 1 is now amended to recite: “an oligonucleotide synthesizer comprising a reaction chamber and a lid, wherein in an open position, said lid provides a substantially enclosed ventilated workspace, *wherein in said open position said ventilated workspace is of sufficient size to permit an operator’s hands to enter said reaction chamber.*” (emphasis added). The Specification provides ample support for this amendment. See, for example, page 21, lines 27-31, and page 22, lines 1-6 of the Specification, describing an embodiment of the present invention such that when the oligonucleotide synthesizer is in an open position (lid open), fumes are collected into a ventilation system, thereby protecting an operator during the normal operation (*e.g.*, hand based reaction support manipulation) of the synthesizer. Embodiments of the ventilated workspace are further described at page 53, lines 7-24, and particularly at lines 11-12, wherein the Specification describes a workspace “designed to allow the instrument operator to reach into the space.”

DeWitt or McGowan do not teach an oligonucleotide synthesizer comprising a reaction chamber and a lid, wherein in a lid open position the lid provides a substantially ventilated workspace, and *wherein in said open position said ventilated workspace is of sufficient size to permit an operator’s hands to enter said reaction chamber.*

Regarding DeWitt, the Examiner states, “As to the limitation of claim 1 stating ‘wherein in an open position, said lid provides a substantially enclosed ventilated workspace,’ the Examiner believes the placement of the manifold over the reservoir block without sealing the device would constitute an ‘open position’ while still allowing for the addition or removal of gas from the block.” Office Action, page 3. The Applicants disagree. However, assuming *arguendo* that this does constitute an open position, Figure 1 of DeWitt, relied upon by the Examiner, demonstrates that the manifold – reservoir block configuration does not constitute a ventilated workspace of sufficient size to permit an operator’s hands to enter the reaction chamber. DeWitt does not anticipate amended Claim 1.

Regarding McGowan, the Examiner relies upon Figures 2 and 3 and columns 3 and 4 of McGowan as anticipating Claim 1. Office Action, page 3. In particular, the Examiner states,

“McGowan teaches a reaction block and a cover...The block contains a base with support holes for holding reaction vials. Covering the block is a two-piece cover assembly comprised of a top cover with four side walls and a top enclosure. The top enclosure contains a hole for a gas tube.” Office Action, pages 3-4. Thus, as described in Figures 2 and 3 and columns 3 and 4 of McGowan, the ventilated workspace is not of sufficient size to permit an operator’s hands to enter the reaction block. McGowan does not anticipate amended Claim 1.

As such, amended Claim 1 is not anticipated by DeWitt or McGowan, and the Applicants requests this rejection be withdrawn.

**C. Claim 20 Is Not Anticipated By McGowan**

The Examiner rejects Claim 20 as being anticipated by McGowan. Office Action, page 3. The Applicants respectfully disagree. However, in order to expedite prosecution, Claim 20 is now amended to further comprise a nucleic acid synthesizer and a vacuum source. The Specification provides ample support for this amendment (See, e.g., Specification, page 14, lines 22-27). While asserting that McGowan teaches the elements of Claims 19 and 20, the Examiner admits that McGowan does not teach a centralized vacuum system. Office Action, page 6. Indeed, McGowan fails to describe the use of any type of vacuum source. As such, Claim 20 as presently amended is not anticipated by McGowan. The Applicants request this rejection be withdrawn.

**III. Rejections Under 35 U.S.C. §103(a)**

The Examiner rejects Claims 5-10 and 21-23 under 35 U.S.C. §103(a). Office Action, page 5. The Applicants respectfully disagree. A *prima facie* case of obviousness requires first, a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference must teach or suggest all the claim limitations. MPEP 2143. As discussed in detail below, the Examiner fails to present a *prima facie* case of obviousness.

**A. Claims 7-10, 21 and 23 Are Non-Obvious**

The Examiner rejects Claims 7 and 8 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 3,986,835 (hereinafter “Takagi”) or U.S. Patent No. 6,485,692 (hereinafter “Freitag”), Claims 9 and 10 under 35 U.S.C. §103(a) as being unpatentable over McGowan or DeWitt, Claim 21 under 35 U.S.C. §103(a) as being unpatentable over McGowan in view of U.S. Patent No. 6,264,891 (hereinafter “Heyneker”), and Claim 23 under 35 U.S.C. §103(a) as being unpatentable over McGowan in view of U.S. Patent No. 5,099,988 (hereinafter “Garra”). Office Action, pages 4-6. The Applicants respectfully disagree. However, without acquiescing to the Examiner's arguments, and in order to expedite prosecution, Claims 7-10, 21, and 23 are now canceled. As such, these rejections are rendered moot. The Applicants reserve the right to prosecute these or similar claims in the future.

**B. Claims 5 And 6 Are Non-Obvious**

The Examiner rejects Claims 5 and 6 under 35 U.S.C. §103(a) as being unpatentable over McGowan or DeWitt. Office Action, page 5. Office Action, page 5. The Applicants respectfully disagree.

McGowan and DeWitt do not teach the use of *nucleic acid* synthesizers. The use of nucleic acid synthesizers present special safety concerns. For example, the Specification, at page 20, lines 13-24, recites:

Whether a system used is open or closed, oligonucleotide synthesis involves the use of an array of hazardous materials, including but not limited to methylene chloride, pyridine, acetic anhydride, 2,6-lutidine, acetonitrile, tetrahydrofurane, and toluene. These reagents can have a variety of harmful effects on those who may be exposed to them. They can be mildly or extremely irritating or toxic upon short-term exposure; several are more severely toxic and/or carcinogenic with long-term exposure. Many can create a fire or explosion hazard if not properly contained. In addition, many of these chemicals must be assessed for emissions from normal operations, *e.g.* for determining compliance with OSHA or environmental agency standards. Malfunction of a system, *e.g.*, as recited above, increases such emissions, thereby increasing the risk of operator exposure, and increasing the risk that an instrument may need to be shut down until risk to an operator is reduced and until any regulatory requirements for operation are met.

Increasing the number of nucleic acid synthesizers increases these safety concerns. Indeed, these safety concerns present a significant obstacle in the art of nucleic acid synthesizers. McGowan and DeWitt do not address *nucleic acid synthesizer* safety issues because they do not teach *nucleic acid* synthesizers.

The Examiner does not present a *prima facie* showing of obviousness. The Examiner alleges, “McGowan and DeWitt, as described above, teach every element... except for a plurality of synthesizers with a reaction chamber and a lid. Both McGowan and DeWitt teach only single reaction blocks. It would have been obvious to one of ordinary skill in the art, however, to provide a plurality of block in a reaction system. The use of a plurality of blocks would provide for the increased production of product.” Office Action, page 5. The Examiner fails to recognize and address the special issues surrounding nucleic acid synthesizers. While “increased production of product” may be a motivating factor for utilizing a plurality of synthesizers, the simultaneous risk inherent with a plurality of nucleic acid synthesizers is a non-motivating factor. Neither McGowan nor DeWitt suggest, teach, or motivate one skilled in the art as to how to handle the safety issues inherent with nucleic acid synthesizers in the pursuit of “increased production of product.” Neither McGowan nor DeWitt teach, suggest, or motivate the combination of a plurality of nucleic acid synthesizers, and the Examiner does not provide a motivation to combine nucleic acid synthesizers that addresses the inherent safety risks with combining nucleic acid synthesizers. As such, the Examiner fails to present a *prima facie* showing of obviousness. The Applicants respectfully request these rejections be withdrawn.

**C. Claim 22 Is Non-Obvious**

The Examiner rejects Claim 22 under 35 U.S.C. §103(a) as being unpatentable over McGowan in light of Heyneker. Office Action, page 6. In particular, the Examiner states, “McGowan...teaches every element...except for a centralized vacuum.” Office Action, page 6. The Examiner next asserts, “Heyneker also teaches an enclosed reaction system. The system is shown in Figure 1 and includes a vacuum system for drawing fluids from the system...It would have been obvious to one of ordinary skill in the art to combine the vacuum system of Heyneker et al. with the block of McGowan. One would add the vacuum system of Heyneker in order to use a vacuum to remove fluids from the system.” Office Action, page 6. The Applicants disagree.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680 (Fed.Cir. 1990). McGowan does not teach, suggest, or motivate a combination with Heyneker.

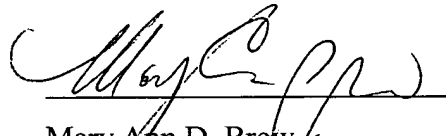
One skilled in the art would not be motivated to combine the vacuum system of Heyneker with McGowan for the removal of fluids because McGowan already teaches a fluid removal system. Indeed, McGowan teaches a synthesizer with a reaction block and a cover that fits over the reaction block. The cover also contains an inlet fixture configured for attachment to a hose that provides pressurized gas, cooling air, and/or fluids into the reaction block. The cover also includes exit openings within the cover for the removal of pressurized gas and fluids. *See, e.g.*, McGowan, column 4, lines 35-49. As such, McGowan provides a fluid removal system. McGowan does not teach, suggest, or motivate modification of this fluid removal system.

The Examiner alleges, “One would add the vacuum system of Heyneker in order to use a vacuum to remove fluids from the system.” Office Action, page 6. The Examiner is not addressing the fact that McGowan already provides a fluid removal system and therefore teaches away from further modification. Absent a teaching, suggestion, or motivation to replace the McGowan fluid removal system with the Heyneker vacuum, the Examiner is combining McGowan with Heyneker merely because they allegedly can be combined. As such, the Examiner is not providing a proper *prima facie* showing of obviousness. The Applicants request this rejection be withdrawn.

## CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicants have addressed all grounds for rejection and Applicants' claims as amended should be passed to allowance. Should the Examiner have any questions, or if a telephone conference would aid in the prosecution of the present application, Applicant encourages the Examiner to call the undersigned collect at 608-218-6900.

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